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10/565,119	01/17/2006	Cinderella Christina Gerhardt	F7718(V)	6138

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EXAMINER	
PANDE, SUCHIRA	

ART UNIT	PAPER NUMBER
1637	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/565,119	GERHARDT ET AL.	
	Examiner	Art Unit	
	Suchira Pande	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-11 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-11 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/18/2006.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112

1. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 10 and 11 provides for the use of cell line derived from a gastric adenocarcinoma, but, since the claim does not set forth any steps involved in the method/process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claims 10 and 11 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Interpretation

3. As indicated above claims 10 and 11 do not spell out the actual use including the active steps of that use that the applicant intends to apply the claimed method for. In view of compact prosecution for searching for prior art, claims 10 and 11 are being interpreted broadly, meaning these cell lines can be used for any possible use that one desires.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

5. Claims 1- 6 and 9-11 are rejected under 35 U.S.C. 102(b) as being anticipated by Atten et al. (2001) Biochemical Pharmacology 62: 1423-1432 as evidenced by Ji et al. (2002) Oncogene 21:6549-6556.

Regarding claim 1, Atten et al. teach in vitro culture of a cell line derived from a gastric adenocarcinoma (see page 1424 section 2.2 where in vitro culture of human gastric adenocarcinoma RF-1 is described), said cell line being capable of producing ghrelin, and said model also comprising a medium suitable for growing said cell line (see page 1424 section 2.2 where media and conditions required to grow RF-1 cells is described).

The in vitro cell culture line taught by Atten et al. is a suitable model for the study of the (regulation of) expression, synthesis and/or secretion of ghrelin is evidenced by teaching of Ji et al. (see title and page 6556 where Ji et al. teach use of these cell lines submitted to ATCC as models). Ji et al. teach comprehensive analysis of gene expression profiles in human gastric cancer cell lines (see abstract). On page 6552, par. 2 Ji et al. teaches gastric carcinoma cell lines (RF1 and RF48). The cell line taught RF-

1 and RF-48 are capable of producing ghrelin is an inherent property of the cell lines themselves. This is evidenced by the fact that in claim 2 Applicant is specifically claiming both the cell lines RF-1 and RF48 as the cell lines useful for model claimed in the instant claim.

Regarding claims 2 & 4, Atten et al. teach wherein the cell line is selected from RF-1 having ATCC number CRL-1864 and RF-48 having ATCC number CRL-1863 (see page 1424 section 2.2 where RF-1 having ATCC number CRL-1864 and RF-48 having ATCC number CRL-1863 are taught).

Regarding claim 3, Ji et al. teach a method for assessing the (regulation of) expression, synthesis of different markers. It is inherently clear to one of ordinary skill in the art that cells have to be grown under appropriate conditions if one wants to examine expression of a specific marker. If one was interested in studying expression of ghrelin from a cell line derived from a gastric adenocarcinoma and capable of producing ghrelin. The one would grow it in a suitable medium. The suitable medium and conditions required are taught by Atten et al. as described above for claim 1. Moreover since Ji et al. teach gene expression profiling of several gastric cell lines including RF1 and RF48, it is inherent that the method taught by them is capable of assessing the (regulation of) expression, synthesis and/or secretion of ghrelin (which as indicated above is an inherent property of the two cell lines taught).

Regarding claim 5, Atten et al. teach wherein the medium is Leibovitz's L15 containing 10% (vol/vol) foetal bovine serum and 2 mM L-glutamine, and wherein the cell line is grown at a temperature of 37.degree. C. in the absence of CO2 (see page

1424 section 2.2.). Atten et al. states the Leibovitz's media taught is supplemented with non-essential amino acids and do not explicitly recite using 2 mM L-glutamine. Glutamine is classified as a non-essential amino acid (see report in Le Magazine published on September 1999 by Greenwell). One of ordinary skill in the art knows that MEM media routinely used for cell culture contains 292 mg/l L-glutamine. Using the formula weight provided by Sigma Aldrich as 146.14 for L-glutamine one can calculate that 292.28 mg of L-glutamine/l media would result in 2 mM L-glutamine. So its clear that one of ordinary skill would add the appropriate amount of L-glutamine as a non essential amino acid to the media taught by Atten et al. Thus all elements of claim 5 are taught by Atten et al.

Regarding claim 6, Atten et al. teach cell culture conditions for the two cell lines taught. They do not explicitly state that, wherein the medium is changed at least every 4 days. However this is a fact that is well known to one of ordinary skill in the art of mammalian tissue cell culture (see Basic Techniques for Mammalian cell tissue culture unit 1.1.2 where Mary C. Phelan describes in step 7. If necessary, feed subconfluent cultures after 3 or 4 days by removing old medium and adding fresh medium.)

Regarding claim 9, Atten et al. teach wherein the cell line is exposed to a variety of test compounds (see title and abstract where exposure to test compound Resveratol (potential chemo preventive candidate against gastric cancer is taught, see page 1430 last par. last line.). Ji et al. evidence that variety of test compounds is indeed routinely used to study responsiveness of each cell line (see Ji et al. page 6551. par. 1). This

teaching inherently requires that cell line under question be exposed to those test compounds).

Regarding claims 10 and 11, Atten et al. teach the use of a cell line derived from a gastric adenocarcinoma that is capable of producing ghrelin when grown in a suitable medium, (claim 10) and the use according to claim 10, wherein the cell line is selected from RF-1 having ATCC number CRL-1864 and RF-48 having ATCC number CRL-1863 (claim 11). (see Atten et al. page 1424 where use of RF-1 having ATCC number CRL-1864 and RF-48 having ATCC number CRL-1863 cell lines is taught).

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claim 7 rejected under 35 U.S.C. 103(a) as being unpatentable over Atten et al. (2001) Biochemical Pharmacology 62: 1423-1432 as evidenced by Ji et al. (2002) Oncogene 21:6549-6556 as applied to claims 1-3 above, and further in view of Chopin et al. (2002) WO 02/090387 A1 published 14 November 2002.

Regarding claim 7, Atten et al. as evidenced by Ji et al. teach method according to claim 3.

Regarding claim 7, Atten et al. as evidenced by Ji et al. do not explicitly spell out wherein the cell line is plated and grown in a culture plate after achieving cell confluence, wherein the plate is stored under the same incubation conditions as those used for growing the cell line (since Atten et. al. teaches media and cell culture conditions used for the cell lines claimed in the present invention it is obvious that above conditions specified are inherently obvious to one of ordinary skill), and wherein ghrelin production is measured using an immunoassay kit.

Regarding claim 7, Chopin et al. teach wherein the cell line is plated and grown in a culture plate after achieving cell confluence (see page 25, lines 24-26 where culture of cells in 96 well plates for 3 days at 37^0C is taught), wherein the plate is stored under the same incubation conditions as those used for growing the cell line (for the purposes of detecting ghrelin which is a small amino acid peptide it is obvious tom one of ordinary skill in the art that the culture plate needs to be stored under conditions where the ghrelin peptide will not be destroyed. Culturing the cells in the media containing Liebovitz's media under the conditions specified in claims 1, 3 and 5 above results in production of ghrelin. Therefore its inherently obvious to one of ordinary skill that storing

the plates containing the produced ghrelin under the same incubation conditions as those used for growing the cell line will not destroy the ghrelin produced.

and wherein ghrelin production is measured using an immunoassay kit (Chopin et al. teach use of three different assays using antibodies raised against ghrelin (see page 24, line 23-25. Therefore by teaching Western blots, immunohistochemistry and ELISA assay for ghrelin using anti-ghrelin antibodies raised against whole human ghrelin peptide, Chopin et al. teach immunoassays that use anti-ghrelin antibodies. Thus Chopin et al. inherently teach all the components required to perform these immunoassays that would be packaged in a kit.

It would have been prima facie obvious to one of ordinary skill to practice the method of Chopin et al. in the method of Atten et al. as evidenced by Ji et al. to measure the ghrelin peptide production by these cells at the time the invention was made. The motivation to do so is provided by Chopin et al. who teach availability of antibodies raised against ghrelin thus providing the reagent required by one of ordinary skill in the art to perform immunoassays to detect ghrelin.

9. Claims 7 and 8 rejected under 35 U.S.C. 103(a) as being unpatentable over Atten et al. (2001) Biochemical Pharmacology 62: 1423-1432 as evidenced by Ji et al. (2002) Oncogene 21:6549-6556 as applied to claims 1-3 above, and further in view of Korbontis et al. (2000) The Journal of Clinical Endocrinology & Metabolism vol. 86: pp 881-887.

Regarding claim 8, Atten et al. as evidenced by Ji et al. teach method according to claim 3.

Regarding claim 8, Atten et al. as evidenced by Ji et al., do not explicitly teach wherein the cell line is used to study ghrelin gene expression, preferably by means of quantitative RT-PCR.

Regarding claim 8, Korbontis et al. teach wherein the tumor cells are used to study ghrelin gene expression (see title and abstract), preferably by means of quantitative RT-PCR (see page 883 section Quantitative RT-PCR.

Regarding claim 7, Korbontis et al. teach Ghrelin RIA that is capable of detecting both octanoylated (active) and non octanoylated (inactive) forms of ghrelin peptide. Thus by teaching the two separate polyclonal antibodies of ghrelin that are useful for detecting the above two forms of ghrelin peptide and their use in RIA, Korbontis et al. teach immunoassay that can be used monitor ghrelin production. By teaching the immunoassay, Korbontis et al. obviously teach all the components of the kit required to detect ghrelin using the immunoassay.

It would have been prima facie obvious to one of ordinary skill in the art to practice the method of Korbontis et al. in the method of Atten et al as evidenced by Ji et al. at the time the invention was made. The motivation to do so is provided to one of ordinary skill by the fact that Korbontis et al. use the Quantitative RT-PCR method to study expression of ghrelin and ghrelin RIA.

They used primary tumor tissues expressing ghrelin as their starting material. Atten et al. as evidenced by Ji et al. teach study of gene expression in gastric

adenocarcinoma cell line using micro arrays. Atten et al. as evidenced by Ji et al. have shown (see supra) that two of the gastric adenocarcinoma cell lines (RF1 and RF48) produce ghrelin. Given the above fact pattern it is obvious to one of ordinary skill in the art that use of Quantitative RT-PCR method of Korbontis et al. will be able to detect ghrelin gene expression in the cell lines claimed. The advantages and ease of working with established cell lines (RF1 and RF48) available through ATCC (ATCC #CRL-1864 and ATCC # CRL-1863) vs. primary tumors tissue are well known to one of ordinary skill well versed in mammalian tissue culture.

Further use of method of Korbontis et al. allows one of ordinary skill to be able to monitor both the gene expression and actual production of ghrelin peptide. Thus enabling one to arrive at comprehensive picture of the various levels of controls (transcriptional and translational) that are operational under given experimental conditions.

Conclusion

10. All claims 1-11 under consideration are rejected.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suchira Pande whose telephone number is 571-272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner
Art Unit 1637

JEFFREY FREDMAN
PRIMARY EXAMINER
5/4/07